REMARKS

Claims 1-22 are currently pending in this application. Claims 1-9 are rejected and claim 21 is objected to. Applicants wish to thank the Examiner for indicating that claims 20 and 22 are directed to allowable subject matter. Claim 21 has been canceled. Claims 25-30 have been added. Support for claims 25-30 can be found, for example, in the claims as filed and in the examples on pages 25-31. Claims 25-30 are directed to methods for promoting neurite outgrowth in a subject. Applicants wish to thank the Examiner for indicating that the specification is enabling for methods of promoting neurite outgrowth. After entrance of the present amendments, claims 1-20 and 25-30 will be pending.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-19 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because practice of the claimed invention allegedly would entail undue experimentation. Applicants respectfully traverse because there is no evidence of record so much as suggesting that those skilled in the art would be unable to practice the claimed invention. Although the Office Action provides a lengthy analysis of certain factors to be considered in assessing whether undue experimentation would be required, close inspection not only reveals that these factors do not support rejection of the present claims but, in fact, indicate that any experimentation associated with the practice of the claimed inventions would be routine in nature and well within the level of skill in the art.

1. BREADTH OF THE CLAIMS

Although the Office Action makes bare assertions that the claims are broad in scope, it fails to provide evidence that their breadth is beyond the level of skill in the art. As noted below, those skilled in the art are quite familiar with methods of using either erythropoietin or fructopyranose sulfamate in methods of treating neurological dysfunction. Given this familiarity, there is no reason to believe that the breadth of the claims would present an impediment to the practice of Applicants' claimed invention.

2. THE STATE OF THE PRIOR ART/PREDICTABILITY OF THE ART

The Office Action makes a bare assertion that the knowledge and level of skill in the art would be insufficient, but fails to cite any references (or otherwise identify evidence) supporting the assertion. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide evidence or technical reasoning substantiating doubts expressed regarding enablement). Instead, the Action states that there are a multitude of diseases and disorders that fall into the category of neurological dysfunction and that the art is silent with regard to the predictability of effectively treating all neurological dysfunctions using the instantly claimed therapy. The Action's position, however, is refuted by the references it cited to support its previous §103(a) rejection (this rejection has since been overcome, see page 2 of the Office Action). For example, in the Office Action mailed August 26, 2003, Paper No. 8, the Action cited three references, Shank *et al.* (WO 00/61138 A1), Sachdeo (Topiramate: Clinical Profile in Epilepsy, Clin Pharmacokinet, May 1998, 34(5):335-346) and Brines *et al.* (WO 00-66164) and stated that the art teaches the use of either erythropoietin or fructopyranose sulfamate for the treatment of neurological disorders:

> It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Shank, Sachdeo, and Brines and obtain a composition comprising a fructopyranose sulfamate (specifically topiramate) and erythropoietin, **each of which are recognized individually for treating neurological disorders**, and administer the combination composition to treat neurological disorders, because the individual active agents are taught to be effective. It requires little more than routine skill in the art to combine art recognized active agents and administer the combined composition to accomplish the same task, **which is to treat neurological disorders and related symptoms and conditions**, since the art discloses these agents are used individually to treat neurological disorders and since Sachdeo provides the suggestion to administer multiple agents **for treating neurological dysfunction**." (Office Action page 4, last paragraph, emphasis added)

Additional references that establish that EPO can be used to treat neurological dysfunction include, for example, Cerami *et al., Nephrol Dial Transplant* 2002; 17 Suppl 1: 8-12 (enclosed as Exhibit A) and Genc *et al., Brain Research,* 2000 19-31 (enclosed as Exhibit B). Cerami *et al* describes the neuroprotective properties of epoietin alfa:

> Thus, systemically administered epoetin alfa in animal models has neuroprotective effects, demonstrating its potential use after brain injury, trauma and multiple sclerosis. It is evident that erythropoietin has biological

> activities in addition to increasing red cell mass. Given the excellent safety profile of epoetin alfa, clinical trials evaluating systemically administered epoetin alfa as a **general neuroprotective treatment** are warranted"
> (abstract, emphasis added)

Genc *et al.* describes the effectiveness of EPO as a neuroprotective agent:

> Multiple models of nervous system injury (mouse, rat, gerbil and rabbit) have been used to demonstrate the effectiveness of EPO as a neuroprotective agent, including focal and global cerebral ischemia, experimental autoimmune encephalomyelitis, kainic acid-induced seizures, experimental traumatic brain injury, neurotoxin-induced experimental Parkinsonism, neonatal hypoxic-ischemic brain injury, subarachnoid hemorrhage, spinal cord ischemia and injury, retinal ischemia, and peripheral nerve injury."
> (page 23, column 1)

The Genc *et al.,* article references a number of other papers that also recognize the connection between the treatment of neurological dysfunction and erythropoietin.

3. THE PRESENCE OR ABSENCE OF WORKING EXAMPLES/QUANTITY OF EXPERIMENTATION

The Office Action also fails to provide any evidence that the number of working examples provided in the specification would be insufficient for those skilled in the art to practice the claimed invention. Although the Office Action notes that the specification does not include examples documenting the use of the compounds of the present invention to treat any and all neurological disorders, such examples are not required as a condition for patentability. In fact, it is well-established that an applicant need not include *any* working examples demonstrating a claimed invention. I*n re Fouche*, 169 U.S.P.Q. 429, 434 (C.C.P.A. 1971. Thus, Applicants' provision of examples demonstrating synergism and the promotion of neurite outgrowth fall far short of demonstrating any lack of enablement.

As is evident from the foregoing analysis, the Office Action's unsupported contentions as to alleged difficulties that those skilled in the art would encounter in practicing the claimed inventions simply do not constitute evidence or technical reasoning of the sort required to substantiate allegations that there is a lack of enablement.

In summary, Applicants submit that the Action has mischaracterized the state of the prior art and the relative skill of those in the art and has improperly rejected the claims as

non-enabled. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 215-568-3100.

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